

Biphasic effects of hormone treatment on risk of cardiovascular disease

RESOLVING THE PARADOX IN POSTMENOPAUSAL WOMEN

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Cardiovascular disease (CVD) caused by atherosclerosis remains the greatest single killer of women, accounting for approximately 40% of total mortality.¹ The current armamentarium of preventive measures against CVD include maintenance of a healthy lifestyle, notably smoking cessation, maintenance of a healthy body weight and regular exercise,²⁻⁴ control or prevention/treatment of hypertension,^{5,6} and appropriate use of medications that lower low-density lipoprotein

cholesterol (LDL-C) and raise high-density lipoprotein cholesterol (HDL-C).^{7,8} However, lifestyle interventions that are effective in highly structured research studies are difficult to sustain in clinical practice. For example, there are high rates of recidivism even after initial success with smoking cessation⁹ or weight loss programs.¹⁰ Anti-hypertensive and lipid-lowering medications may be expensive and have a variety of adverse effects, and noncompliance is often an issue. Moreover, approximately half of patients with a first CVD event would not have been candidates for lipid-lowering medications based on current guidelines for LDL cholesterol-lowering medication, which has led to recommendations for reducing the target LDL level.¹¹ Further, lipid medica-

tions allow a majority of CVD events to occur.¹² Given the above, the problem of CVD prevention in older women remains a pressing, unresolved issue.

Regularly ovulating women of reproductive age are significantly protected against CVD compared with men, but CVD increases within 10 years of menopause to levels matching or exceeding incidence rates among men,¹³ suggesting that ovarian estrogen may help protect women against atherosclerosis. This observation led to the corollary hypothesis that treatment of postmenopausal women with estrogens (menopausal hormone therapy [MHT]) might prevent the postmenopausal increase in CVD rates. Yet, despite more than 30 years of research attempting to define whether and how postmenopausal estrogen replacement might protect women against CVD, the issue remains uncertain and, indeed, controversial.

Progression of atherosclerosis

Atherosclerosis is a progressive pathological process characterized by the formation of plaques in the arterial wall, typically at sites of endothelial injury, frequently at arterial branch

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